PATENT COOPERATION TREATY

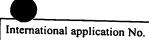
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PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference B 3366 PCT	FOR FURTHER ACTION S	ee Notification of Transmittal of International reliminary Examination Report (Form PCT/IPEA/416)				
International application No. PCT/EP98/07909	International filing date (day/mor	nth/year) Priority date (day/month/year)				
International Patent Classification (IPC) or na C12Q 1/68	04 December 1998 (04.1	2.98) 05 December 1997 (05.12.97)				
Applicant MAX-PLANCK-GESELLS	CHAFT ZUR FÖRDERUN	G DER WISSENSCHAFTEN E.V.				
 This international preliminary exam Authority and is transmitted to the ap This REPORT consists of a total of	pheant according to Article 36.	d by this International Preliminary Examining				
This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).						
These annexes consist of a total of sheets.						
3. This report contains indications relating to the following items:						
Basis of the report						
II Priority						
	and industrial applications					
<u></u>	,					
Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;						
VI Certain documents cited						
VII Certain defects in the	VII Certain defects in the international application					
VIII Certain observations on the international application						
Date of submission of the demand	Date of com	upletion of this report				
17 June 1999 (17.06.99		08 February 2000 (08.02.2000)				
Name and mailing address of the IPEA/EP	Authorized	officer				
Facsimile No.	Telephone N	No.				



PCT/EP98/07909

I. Basis of the report		
This report has been draw under Article 14 are referred	n on the basis of (Replacement shift to in this report as "originally filed	neets which have been furnished to the receiving Office in response to an invitation d" and are not annexed to the report since they do not contain amendments.):
the internation	nal application as originally filed	d
the description	n, pages1 - 29	, as originally filed,
	pages	, filed with the demand,
	pages	, filed with the letter of
		, filed with the letter of
the claims,	Nos.	, as originally filed,
		, as amended under Article 19,
	Nos	, filed with the demand,
	Nos. 1 - 18	, filed with the letter of
	Nos.	, filed with the letter of
the drawings,	sheets/fig1/6 - 6/6	
	sheets/fig	
		, filed with the letter of,
	sheets/fig	, filed with the letter of
	pages	
the claims,	Nos.	
the drawings,	sheets/fig	
This report has been e to go beyond the disci	mod, as indicated in th	mendments had not been made, since they have been considered the Supplemental Box (Rule 70.2(c)).

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Statement			
Novelty (N)	Claims	1-18	YES
	Claims		NO NO
Inventive step (IS)	Claims	1-17	YES
	Claims	18	NO
Industrial applicability (IA)	Claims	1-18	YES
	Claims		NO

- 2. Citations and explanations
 - 1. Attention is drawn to the following documents:

D1: Arlinghaus et al., Anal. Chem., Vol. 69, pp. 1510-1517 (April 15, 1997);

D2: Reddy et al., Anal. Biochem., Vol. 220, pp. 200-207 (1994);

D3: Little et al., J. Am. Chem. Soc., Vol. 116, pp. 4893-4897 (1994).

2. Novelty (PCT Article 33(2))

The invention relates to a method of identifying a nucleotide sequence in a nucleic acid molecule by means of predetermined probes of differing mass, using electrospray-mass spectrometry (Claims 1 to 17). It also relates to a kit containing the probes and a sample holder (Claim 18).

The subject matter of independent Claims 1 and 18 appears to be novel over the known prior art. Claims 2 to 17 are therefore also novel.

- 3. Inventive step (PCT Article 33(3))
- a. Document D1 is considered to be the prior art closest to the subject matter of Claims 1 to 17. It discloses hybridization sequencing, where a known oligonucleotide hybridizes with a known DNA which is immobilized on a solid phase. The probes are labelled with mass tags (tin isotopes). After a hybridization stage, the solid phase is washed. The bond between the tin atom and the probe is opened, so that the free tin atom can be detected by resonance ionization mass spectrometry (p. 1513, column 1).

The subject matter of Claim 1 differs from D1 by steps (c) and (d), that is to say, the separation of the specifically hybridized probes into a solvent, and the analysis of the hybridized probes in solution by electrospray-mass spectrometry (ES-MS). The problem addressed by the invention was therefore to provide an alternative method of identifying hybridized probes. ES-MS is already known as a method of analyzing oligonucleotides (D2, D3). D2 also states that ES-MS can be routinely used to analyze modified oligodesoxynucleotides (p. 201, column 1). The invention goes beyond a simple combination of two known methods, however. There is, furthermore, no suggestion to a skilled person that ES-MS is even suitable for the D1 methods.

The subject matter of Claim 1 therefore appears to be inventive. It follows that Claims 2 to 17 are also inventive.

b. The subject matter of Claim 18 does not appear to be

inventive. A sample holder which is pretreated and thereby allows the bonding of target DNAs is a routine technical measure (cf. D1, p. 1510). Probe sets with mass tags are also known (cf. D1, p. 1511, column 1). Although D1 does not disclose a kit, to a skilled person it is standard practice to pack the known components into a kit.

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Claim 9 is dependent on Claims 6 to 8, amongst others, although it has a wider scope of protection. The feature "wherein the probes are modified nucleic acid molecules" in Claim 9 also encompasses possible modification with a mass tag (as in Claims 6 to 8). Claim 9 is therefore unclear (PCT Article 6).